Please replace the paragraph beginning at line 30 of page 17 with the following rewritten paragraph:

Multiple alignment of PKARs. The M. circinelloides PKAR was aligned with other fungal PKAR sequences. Identical residues are boxed. Abbreviations and accession numbers: Mcir: M. circinelloides, AJ400723 (EMBL) (SEQ ID NO:36); Anig: Aspergillus niger, Q9C196 (SwissProt) (SEQ ID NO:37); Beme: Blastocadiella emersonii, P31320 (SwissProt) (SEQ ID NO:38); Calb: C. albicans Q9HEW1 (SwissProt) (SEQ ID NO:39); Scer: S. cerevisiae, P07278 (SwissProt) (SEQ ID NO:40), Spom: Schizosaccharomyces pombe, P36600 (SwissProt) (SEQ ID NO:41); Mrou: M. rouxii, Q9P8K6 (SwissProt) (SEQ ID NO:42).

Please replace the paragraph beginning at line 5 of page 8 with the following rewritten paragraph:

Alignment of M. circinelloides PKAC with other fungal counterparts. Identical residues are boxed. Abbreviations and accession numbers: M.cir: M. circinelloides, ~~AJ400723~~ AJ431364 (EMBL) (SEQ ID NO:43); Anig: A. niger, P87077 (SwissProt) (SEQ ID NO:44); Beme: B. emersonii, Q12741 (SwissProt) (SEQ ID NO:45); Calb: C. albicans Q9HEW0 (SwissProt) (SEQ ID NO:46); Scer: S. cerevisiae, P06245 (SwissProt) (SEQ ID NO:47), Spom: S. pombe, P40376 (SwissProt) (SEQ ID NO:48).

Please replace the paragraph beginning at line 23 of page 18 with the following rewritten paragraph:

Overexpression of PKAR in M. circinelloides. A: Plasmid map (left) of pEUKA4-pkaR. Northern blot analysis (middle panel) of KFA121 (a pEUKA4-pkaR transformant) grown in YNB medium with 5 % glucose (lane 2). The same conditions were used for the control strain KFA89 (lane 1). The RNA gel is shown below for loading control. Primer extension analysis (right panel): the fragment obtained is indicated with an arrow; a sequence ladder was run on pEUKA4-pkaR to determine the transcription start site (tss). The sequence obtained (SEQ ID NO:49) is shown below (the arrow indicates the tss; mRNA sequence is shown in italics, cloning site (*XhoI*) and ATG start codon of *pkaR* (bold). B: Colony morphology of KFA121 (right) and KFA89 (left) on YNB plates (2 % glucose) showing the higher branching degree of KFA121.

Please replace the paragraph beginning at line 6 of page 19 with the following rewritten paragraph:

The M. circinelloides STE12 and MPK1 homologues. A: The protein sequence corresponding to the identified M. circinelloides *ste12* fragment was aligned with relevant fungal STE12 sequences. Abbreviations and accession numbers: Mcir: M. circinelloides, AJ4007234 (EMBL) (SEQ ID NO:50); A.nid: A. nidulans, O74252 (SwissProt) (SEQ ID NO:54); Calb: C. albicans P43079 (SwissProt) (SEQ ID NO:52); Scer: S. cerevisiae, P13574 (SwissProt) (SEQ ID NO:51); Klac (SEQ ID NO:53); Cpur (SEQ ID NO:55). B: The protein sequence corresponding to the

identified M. circinelloides *mpk1* fragment (MPK1) was aligned with relevant fungal STE12 sequences. Abbreviations and accession numbers: Mcir: M. circinelloides, ~~AJ400723~~ AJ309731 (EMBL) (SEQ ID NO:56); Calb (MKC1): C. albicans P43068 (SwissProt) (SEQ ID NO;58); Scer (SLT2): S. cerevisiae, Q00772 (SwissProt) (SEQ ID NO:60), Spom (SPM1): S. pombe, Q92398 (SwissProt) (SEQ ID NO:57); FMK1 (SEQ ID NO:59); ERK1 (SEQ ID NO:61).

Please replace the paragraph beginning at line 18 of page 19 with the following rewritten paragraph:

Nucleotide sequence (SEQ ID NO:24) and derived amino-acid sequence (SEQ ID NO:25) of *gpd1*. Numbering of nucleotides is with respect to the start of the coding sequence. Exon sequences are capitalised. Sequences with homology to the lariat formation consensus sequence within introns are italicised. Putative TATA and CAAT boxes are boxed and bolded, respectively. Pyrimindine stretch is underlined. The putative polyadenylation signal is double underlined. The transcription start point is capitalised and bolded. The sequence corresponding to the gene-specific oligonucleotide used in Northern blotting and primer extension is wavy underlined.

Please replace the paragraph beginning at line 19 of page 47 with the following rewritten paragraph:

Many putative downstream effectors of the small GTPases Cdc42 and Rac contain a GTPase binding domain (GBD), also called p21 binding domain (PBD), which has been shown to specifically bind the GTP bound form of Cdc42 or Rac, with a preference for Cdc42. The most conserved region of GBD/PBD domains is the N-terminal Cdc42/Rac interactive binding motif (CRIB), which consists of about 16 amino acids with the consensus sequence I-S-X-P-X(2,4)-F-X-H-X(2)-H-V-G (SEQ ID NOs:62-63). Although the CRIB motif is necessary for the binding to Cdc42 and Rac, it is not sufficient to give high-affinity binding.

Please replace the paragraph beginning at line 30 of page 51 with the following rewritten paragraph:

The term catalytic domain as used herein above shall include the conserved TXY motif in which both the threonine and tyrosine residues are phosphorylated during activation of the enzyme by upstream dual-specificity MAP kinase kinases (MAPKKs). In addition to the TXY motif, other motifs include the region located just after the TXY motif and containing a F and a C residue that are MAPK-specific. The R and E residues in the first part of the pattern, and the R, D and K residues in the second part, are shared by many additional protein kinases. They have been included in the pattern to eliminate matches from unrelated sequences in the database, and to "anchor" the MAPK-specific F and C residues to this region.

Accordingly, one preferred catalytic domain comprises the consensus pattern: F-x(10)-R-E-x(72,86)-R-D-x-K-x(9)-C (SEQ ID NOs:64-65), and this domain is preferably recognised by an antibody used to define fragments of MAPK in accordance with the present invention.

Please replace the paragraph beginning at line 8 of page 120 with the following rewritten paragraph:

The protein sequences of several fungal regulatory subunits of protein kinase A (PKAR) are present in the public databases. The high level of sequence homology allowed the design of degenerate primers (Table 1) derived from the GDFFYVVE and WALDRNTS regions (positions 2193-2260 and 2766-2793 in the M. circinelloides PKAR protein sequence (SEQ ID NO:2), see below) and the PCR amplification of a 183-bp fragment, named pkaR13b-1. Sequence analysis and database searches identified pkaR13b-1 as highly homologous to known fungal and eukaryotic PKAR encoding genes. Using pkaR13b-1 as a probe, a positive clone, pkaR1, was identified from a M. circinelloides genomic library. Sequence analysis of the 2-kb insert in pkaR1 showed that it contained a chromosomal insert encompassing the full-length M. circinelloides *pkaR* gene including 40-bp upstream of the ATG start codon. Further cloning using inverse PCR allowed the characterisation of the upstream region of *pkaR* including 541 bp of the promoter region (Fig. 3).

Please replace the paragraph beginning at line 14 of page 121 with the following rewritten paragraph:

The M. circinelloides PKAR displays an overall homology to other fungal PKARs (31-45 % identity, Fig. 4) and contains the expected well-conserved domains. Thus, two domains with a high degree of homology to cAMP-binding domains in other PKARs (94 to 64 % identity), are present in the M. circinelloides PKAR (sFGELALmynAPRAATii and yFGELALlndAPRAATvv, at positions 247-264 and 369-386, respectively, in the amino acid sequence, Fig. 4). Further, a putative kinase inhibitor domain (RRTSVK) is found at position 144-149 in the amino acid sequence (SEQ ID NO:36) (Fig. 4). The partial sequence available from the PKAR of the related fungus M. rouxii does not include this domain (Sorol et al., 2000) and therefore comparison of the PKAR kinase inhibitor domain between these two Mucor species awaits.

Please replace the paragraph beginning at line 7 of page 122 with the following rewritten paragraph:

The *pkaC* gene contains two putative introns in the 5' end and putatively encodes a protein of 605 amino acid residues. This protein contains an ATP-binding domain (GQGSVG at position 254-259 in the amino acid sequence (SEQ ID NO:43), Fig. 5) and a region with high homology to a serine/threonine protein kinase active site (position 367-379 in the amino acid sequence). Surprisingly, the conserved active site aspartic

acid residue found in other PKACs is in M. circinelloides replaced by an aspargine residue. The codon encoding the aspargine residue (AAC) was confirmed by sequencing of different independent PCR products. However, we cannot completely rule out the possibility that this divergence is due to a PCR amplification artefact.

Please replace the paragraph beginning at line 3 of page 126 with the following rewritten paragraph:

STE12 is a transcription factor that participates in the MAPK-dependent signal transduction pathway in S. cerevisiae, C. albicans and C. neoformans leading to filamentation (Liu et al., 1994, Yue et al., 1999). In C. albicans, a *ste12* null mutant strain is defective in filamentation (Liu et al., 1994). The STE12 transcription factor consists of a N-terminal region involved in DNA binding, a central induction domain and a C-terminal region involved in transcriptional activation. To investigate whether M. circinelloides possesses a *ste12* homologue, PCR was carried out using degenerate primers designed from the most conserved sequence of the N-terminal region of available *ste12* genes (KFFLATA and QKKQKVF, positions 44-50 and 151-157 in the S. cerevisiae STE12 protein sequence (SEQ ID NO:51), Fig. 9A). A 384-bp fragment, ste12b-1, was obtained using R7B DNA as template. Sequence analysis revealed a high degree of homology between the protein sequence encoded by the ste12b-1 DNA

sequence and other fungal STE12 homologues (56-64%, Fig. 9A), confirming that the cloned fragment is part of the M. circinelloides *ste12* gene.

IN THE SEQUENCE LISTING

Please substitute the attached Sequence Listing, numbered as pages 1-72 for the Sequence Listing previously submitted.

REMARKS

1. Applicants hereby submit the following:

[ ] a paper copy of a "Sequence Listing", complying with §1.821(c), to be incorporated into the specification as directed above;

[XX] an amendment to the paper copy of the "Sequence Listing" submitted on March 8, 2002, the amendment being in the form of substitute sheets;

[XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;